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Electronical Supplementary Information

The Impact of the Counterion in the Performance of Ionic Hydrotropes

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S1. Experimental Details

S1.1 Chemicals

The abbreviation, source, and purity of the compounds used in this work are listed in Table S1. All compounds were used as supplied. Ultrapure water obtained using a Milli-Q plus 185 water purification apparatus (resistivity of 18.2 MΩ·cm at 298 K and total organic carbon inferior to 5 $\mu g \cdot dm^{-3}$) was used to prepare all aqueous solutions. Even though gallic acid monohydrate was here experimentally used, all results are reported and analysed in terms of anhydrous gallic acid.

Table S1. *The abbreviation, CAS number, source, and purity (wt%) of the compounds used in this work.*

Compound	**Abbreviation**	**CAS Number**	**Source**	**Purity (wt%)**
1-Butyl-3-methylimidazolium chloride	$[C_4C_1im]Cl$	79917-90-1	Iolitec	99.0
1-Butyl-3-methylimidazolium dicyanamide	$[C_4C_1im][DCA]$	448245-52-1	Iolitec	98.0
1-Butyl-3-methylimidazolium thiocyanate	$[C_4C_1im][SCN]$	344790-87-0	Iolitec	98
1-Butyl-3-methylimidazolium *p*-toluensesulfonate	$[C_4C_1im][TOS]$	410522-18-8	Iolitec	98
Sodium *p*-toluenesulfonate	Na[TOS]	657-84-1	TCI	> 90.0
Caffeine	———	58-08-2	Fluka	> 99
Gallic Acid Monohydrate	———	5995-86-8	Merck	> 99.5
Vanillin	———	121-33-5	Sigma Aldrich	99
Syringic Acid	———	530-57-4	Acros Organic	>97.0
Naproxen	———	22204-53-1	TCI	99
Ibuprofen	———	15687-27-1	Sigma Aldrich	98
Ammonium acetate	———	631-61-8	Sigma Aldrich	99.99
Acetic acid	———	64-19-7	Sigma Aldrich	99.99
Acetonitrile	———	75-05-8	Fisher	99.99

S1.2 Solubility Measurements

The solubility curves of the solutes in the hydrotropic systems studied were experimentally determined using the isothermal shake-flask method.[1] First, water/hydrotrope solutions were prepared to cover the entire composition range of the system, from pure water to the aqueous solubility limit of the hydrotrope. Then, excess solute was added to each solution and the samples were left to equilibrate under constant agitation (1050 rpm) at 303.2 ± 0.5 K for 72 h, using an Eppendorf Thermomixer Comfort apparatus. After equilibration the samples were centrifuged at (303.2 ± 0.5) K at (4500 rpm) for 20 minutes, using a Hettich Mikro 120 centrifuge. Finally, samples of the liquid phase were carefully collected for solute quantification. This procedure was repeated at least three times for each hydrotrope concentration. In the cases of naproxen and ibuprofen, the samples were collected using syringe filters (0.45 nm) to remove possible suspended particles.

In the case of caffeine, gallic acid, syringic acid, and vanillin, the concentration of the solute was quantified using by UV spectroscopy using a SHIMADZU UV-1700 Pharma-Spec spectrometer at appropriate wavelengths (272 nm for caffeine, 262 nm for gallic acid, 267 nm for syringic acid, and 280 nm for vanillin). In the case of naproxen and ibuprofen, the concentration of the solute was quantified using HPLC. To do so, the samples are diluted in a mixture of acetonitrile and water with a volume ratio of 30:70. Then the concentration of the solute is measured using HPLC-DAD (HPLC Elite LaChrom, VWR Hitachi, with a diode array detector l-2455) at wavelengths 230 nm, as previously described in literature.[2] The mobile phase used in the HPLC analysis was composed of 5 mM of ammonium acetate in pH 4 (the pH adjustment was made by the addition of acetic acid) and 5 wt% of acetonitrile. The flow rate was 0.8 $\mathrm{mL \cdot min^{-1}}$ and the injection volume was 10 µL. Each sample was analysed at least twice.

S1.3 Detailed Results

The experimental solubility results obtained in this work are reported below in Tables S2-S10.

Table S2. *The aqueous solubility (S) of the solutes studied in this work at (303.2 ± 0.5) K, along with the standard uncertainty (s).*

Solute	*S* /mM	*s* /mM	Solute	S /mM	*s* /mM
Caffeine	118.4	5.2	Syringic Acid	7.5	0.4
Gallic Acid	82.4	2.4	Naproxen	0.138	0.005
Vanillin	86.0	4.5	Ibuprofen	0.182	0.009

Table S3. *The solubility of caffeine (S) in aqueous solutions of Na[TOS], [C_4C_1im]Cl, and [C_4C_1im]TOS, at (303.2 ± 0.5) K, along with the standard uncertainty (s).*

Na[TOS]			[C_4C_1im]Cl			[C_4C_1im][TOS]		
wt%	*S* /mM	*s* /mM	wt%	*S* /mM	*s* /mM	wt%	*S* /mM	*s* /mM
0.048	228	3.3	0.045	143	2.7	0.078	230	1.6
0.094	261	8.2	0.088	152	9.1	0.153	266	1.8
0.140	277	14	0.132	163	9.7	0.228	275	9.1
0.184	301	12	0.175	169	1.7	0.300	294	6.3

Table S4. *The solubility of gallic acid (S) monohydrate in aqueous solutions of Na[TOS], [C_4C_1im]Cl, and [C_4C_1im]TOS, at (303.2 ± 0.5) K, along with the standard uncertainty (s).*

Na[TOS]			[C_4C_1im]Cl			[C_4C_1im][TOS]		
wt%	*S* /mM	*s* /mM	wt%	*S* /mM	*s* /mM	wt%	*S* /mM	*s* /mM
0.035	98	3.6	0.010	110	5.0	0.010	101	2.9
0.040	101	2.0	0.020	128	2.2	0.020	122	4.1
0.050	106	3.5	0.030	158	2.9	0.031	143	3.1
0.065	115	1.2	0.040	175	9.0	0.040	167	6.1
0.101	149	0.6	0.050	187	1.7	0.050	179	5.8
0.131	167	8.4	0.071	272	1.7	0.100	261	3.5
0.163	196	3.9	0.100	364	20	0.289	722	13
0.201	238	8.0	0.120	404	4.5	0.400	932	82
0.240	268	9.6	0.150	508	28	0.512	1175	120
0.300	288	15	0.200	716	74			
			0.302	919	17			
			0.400	1271	34			

Table S5. *The solubility of vanillin (S) in aqueous solutions of Na[TOS] and [C_4C_1im]Cl, at (303.2 ± 0.5) K, along with the standard uncertainty (s).*

Na[TOS]			[C_4C_1im]Cl		
wt%	***S* /mM**	***s* /mM**	**wt%**	***S* /mM**	***s* /mM**
0.010	95	1.0	0.010	106	3.9
0.020	106	0.7	0.020	115	1.6
0.030	122	1.5	0.030	131	4.5
0.040	131	0.7	0.040	145	5.9
0.050	150	14	0.050	164	6.0
0.100	228	9.9	0.100	243	34
0.151	395	8.6	0.200	586	91
0.200	556	12	0.251	1086	21
0.246	825	9.7	0.294	1554	43
0.299	1068	12			
0.332	1181	12			
0.400	1315	18			

Table S6. *The solubility of syringic acid (S) in aqueous solutions of Na[TOS], [C_4C_1im]Cl, and [C_4C_1im]TOS, at (303.2 ± 0.5) K, along with the standard uncertainty (s).*

Na[TOS]			[C_4C_1im]Cl			[C_4C_1im][TOS]		
wt%	***S* /mM**	***s* /mM**	**wt%**	***S* /mM**	***s* /mM**	**wt%**	***S* /mM**	***s* /mM**
0.010	12.4	1.6	0.010	1.0	0.14	0.010	11.3	0.30
0.020	14.6	3.4	0.020	1.2	0.21	0.020	15.2	0.10
0.030	16.7	1.3	0.030	1.3	0.65	0.030	21.7	0.55
0.040	20.1	0.72	0.040	1.5	0.76	0.040	31.8	1.2
0.051	23.5	0.38	0.050	1.9	0.11	0.050	42.2	2.5
0.102	40.6	1.4	0.100	3.1	0.27	0.100	238.2	1.2
0.206	88.2	4.8	0.294	16.2	2.3	0.199	426.5	2.2
0.302	149.9	2.7	0.395	28.3	1.6	0.289	724.0	3.7
						0.405	937.3	4.7
						0.512	1114.4	5.6
						0.596	1276.7	6.4

Table S7. *The solubility of naproxen (S) in aqueous solutions of Na[TOS], [C_4C_1im]Cl, and [C_4C_1im]TOS, at (303.2 ± 0.5) K, along with the standard uncertainty (s).*

Na[TOS]			[C_4C_1im]Cl			[C_4C_1im][TOS]		
wt%	***S* /mM**	***s* /mM**	**wt%**	***S* /mM**	***s* /mM**	**wt%**	***S* /mM**	***s* /mM**
0.050	0.82	0.002	0.010	0.20	0.005	0.049	0.36	0.006
0.100	1.52	0.006	0.020	0.25	0.004	0.100	0.86	0.006
0.150	2.45	0.010	0.030	0.33	0.006	0.151	1.90	0.010
0.200	3.60	0.017	0.040	0.41	0.010	0.203	3.90	0.013
0.364	13.26	0.026	0.050	0.50	0.010	0.400	12.75	0.012
0.450	19.95	0.028	0.100	1.05	0.015	0.597	114.86	0.015
			0.149	1.82	0.016			
			0.200	2.66	0.017			
			0.399	12.56	0.020			

Table S8. *The solubility of ibuprofen (S) in aqueous solutions of Na[TOS], [C_4C_1im]Cl, and [C_4C_1im]TOS, at (303.2 ± 0.5) K, along with the standard uncertainty (s).*

Na[TOS]			[C_4C_1im]Cl			[C_4C_1im][TOS]		
wt%	***S* /mM**	***s* /mM**	**wt%**	***S* /mM**	***s* /mM**	**wt%**	***S* /mM**	***s* /mM**
0.300	5.94	0.29	0.010	0.21	0.006	0.010	0.20	0.004
0.400	17.91	0.89	0.020	0.26	0.007	0.021	0.28	0.004
0.451	30.11	1.5	0.030	0.29	0.004	0.030	0.33	0.007
			0.040	0.31	0.003	0.040	0.42	0.009
			0.400	5.51	0.18	0.500	79.82	0.023
						0.600	341.82	0.024

Table S9. *The solubility of naproxen (S) in aqueous solutions of [C_4C_1im][SCN] and [C_4C_1im][DCA], at (303.2 ± 0.5) K, along with the standard uncertainty (s).*

[C_4C_1im][SCN]			[C_4C_1im][DCA]		
wt%	***S* /mM**	***s* /mM**	**wt%**	***S* /mM**	***s* /mM**
0.005	0.32	0.004	0.005	0.33	0.004
0.010	0.48	0.006	0.010	0.45	0.005
0.020	0.84	0.007	0.020	0.76	0.006
0.031	1.15	0.010	0.030	1.02	0.007
0.040	1.54	0.010	0.040	1.42	0.008
0.050	2.01	0.013	0.051	2.01	0.010
0.100	4.42	0.015	0.101	5.47	0.011
0.150	8.47	0.018	0.153	8.67	0.015
0.200	14.60	0.021	0.202	14.42	0.014
0.400	70.25	0.020	0.300	47.73	0.016
			0.400	81.93	0.018

Table S10. *The solubility of ibuprofen (S) in aqueous solutions of [C_4C_1im][SCN] and [C_4C_1im][DCA], at (303.2 ± 0.5) K, along with the standard uncertainty (s).*

[C_4C_1im][SCN]			[C_4C_1im][DCA]		
wt%	***S* /mM**	***s* /mM**	**wt%**	***S* /mM**	***s* /mM**
0.031	1.40	0.014	0.030	1.78	0.009
0.040	1.78	0.006	0.040	2.59	0.012
0.401	59.07	0.028	0.308	36.75	0.031

S2. Cooperative Hydrotropy Model

S2.1 Fitted Model

Shimizu and Matubayasi[3] have developed a statistical thermodynamics-based model that describes the solubility enhancement of a hydrophobic solute due to the presence of a hydrotrope. This model can be expressed in its linearized form as:

$$\ln\left(\frac{1-\frac{S}{S_0}}{\frac{S}{S_0}-\left(\frac{S}{S_0}\right)_{max}}\right) = m \cdot \ln(x_H) + b \tag{S1}$$

where S is the molar solubility of the solute in the aqueous hydrotrope solution, S_0 is the molar solubility of the solute in pure water, $(S/S_0)_{max}$ is the maximum attainable relative solubility of the solute in the aqueous hydrotrope solution (henceforth δ_{max}), x_H is the mole fraction of the hydrotrope in the final, ternary (water/hydrotrope/solute) mixture, and m and b are parameters of the model. Equation S1 requires the mole fraction of the hydrotrope to be known in the ternary mixture at equilibrium. This is calculated using the following expression:

$$x_H = \frac{\frac{(1000\cdot\rho - S\cdot M_S)\cdot w_H}{M_H}}{\frac{(1000\cdot\rho - S\cdot M_S)\cdot(1-w_H)}{M_{H_2O}} + \frac{(1000\cdot\rho - S\cdot M_S)\cdot w_H}{M_H} + S} \tag{S2}$$

where ρ is the density (g·mL^{-1}) of the ternary mixture, M_{H_2O}, M_H, and M_S are the molar masses of water, the hydrotrope, and the solute, respectively, and w_H is the mass fraction of the hydrotrope in the binary hydrotrope/water solvent (solute-free basis). Since the maximum solubility of the solute was not reached using the hydrotrope concentrations studied in this work, δ_{max} was left as an adjustable parameter of the model. The results of the fitting of the model are depicted in Figures S1-S6 and the parameters are reported in Table S11.

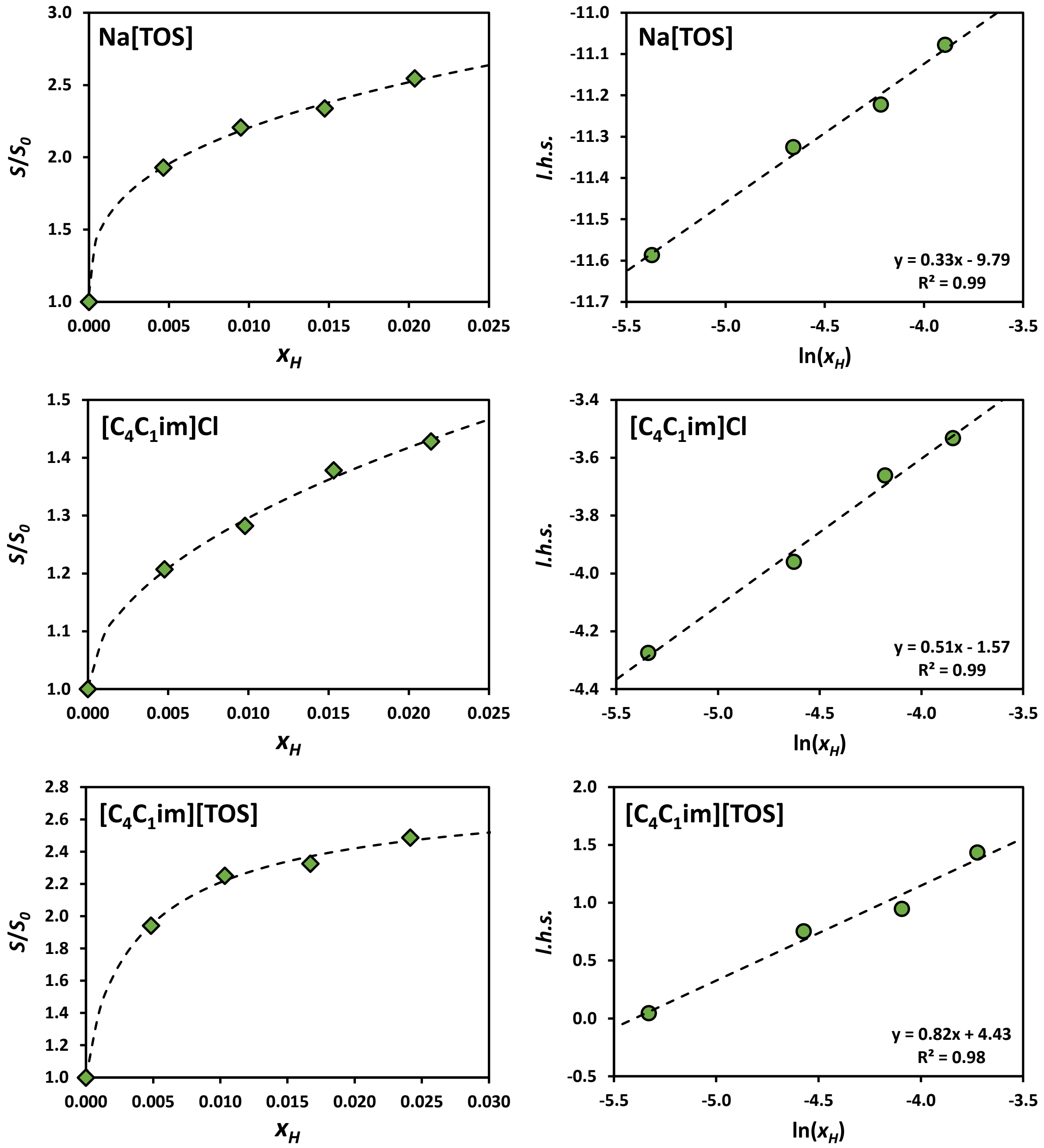

Figure S1. ***Left:*** *solubility enhancement (S/S_0) of caffeine in aqueous solutions of ionic hydrotropes (◆) along with the fitted curve (dashed line) obtained using the cooperative hydrotropy model.* ***Right:*** *the linearized form of the cooperative hydrotropy model for each hydrotropic system, where the vertical axis is the left-hand side of Equation S1 and the dashed line is the straight line obtained using the method of least squares.*

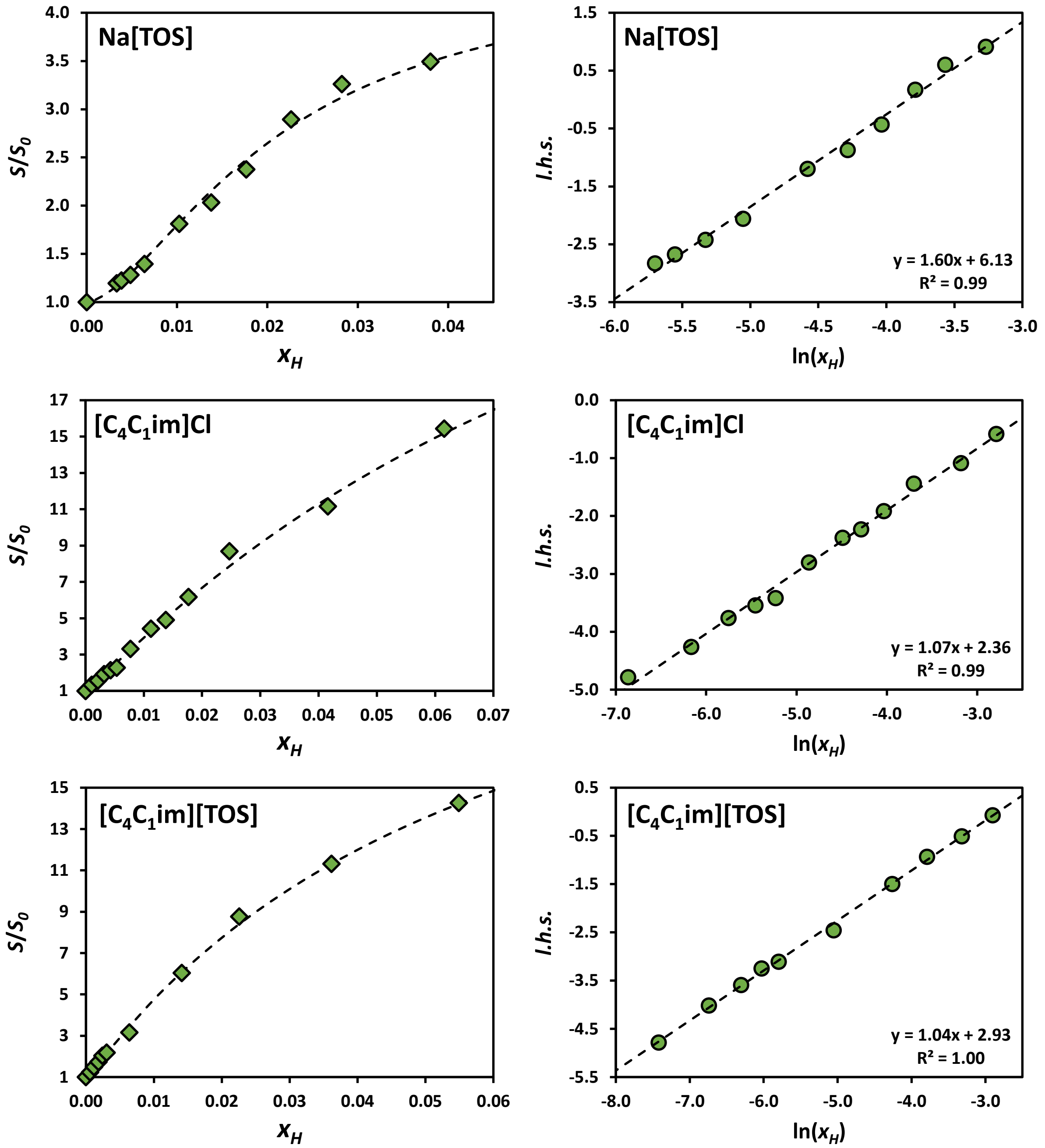

Figure S2. ***Left:*** *solubility enhancement (S/S_0) of gallic acid in aqueous solutions of ionic hydrotropes (◆) along with the fitted curve (dashed line) obtained using the cooperative hydrotropy model.* ***Right:*** *the linearized form of the cooperative hydrotropy model for each hydrotropic system, where the vertical axis is the left-hand side of Equation S1 and the dashed line is the straight line obtained using the method of least squares. Data measured in this work or taken from the literature.*[4]

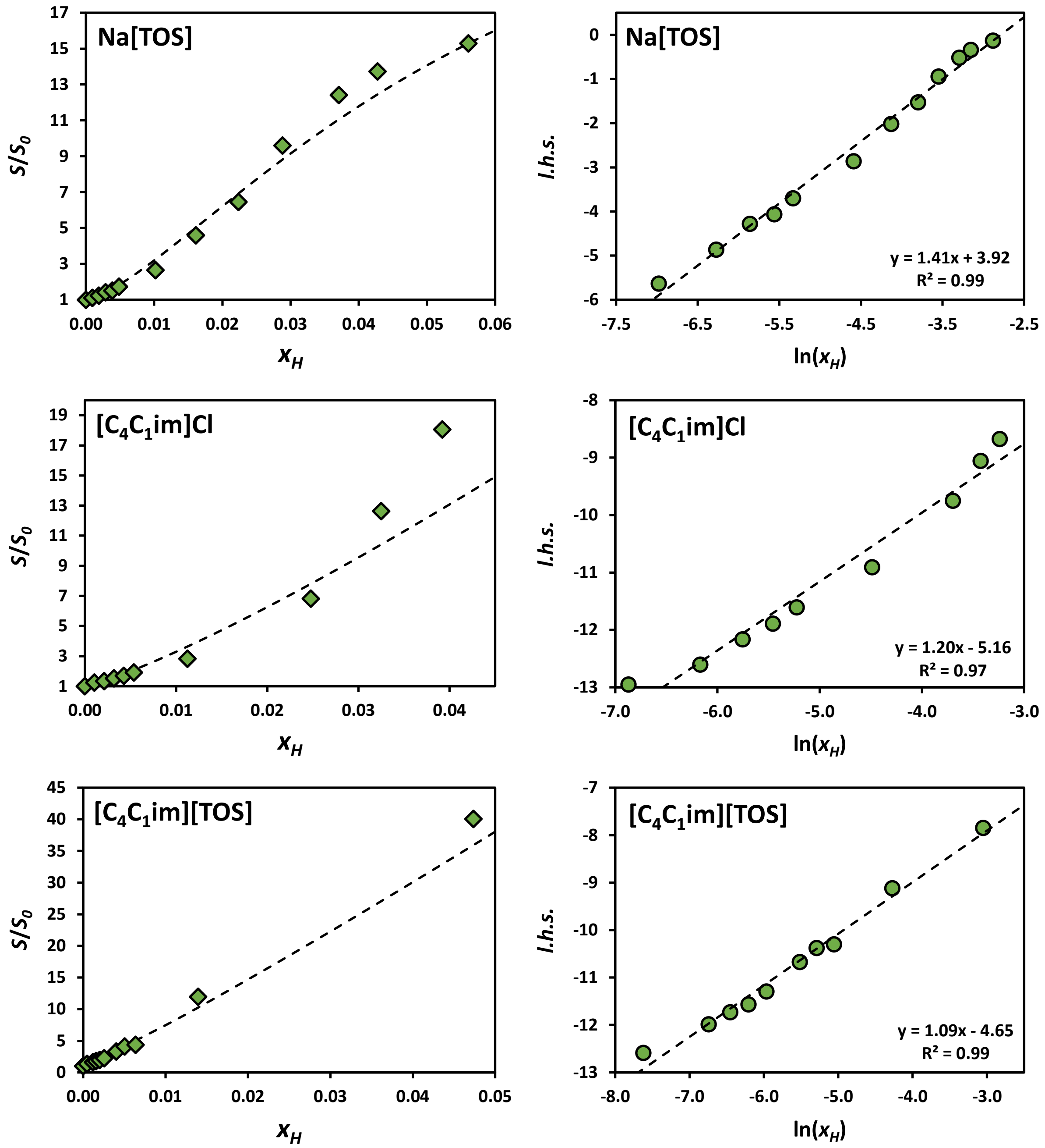

Figure S3. ***Left:*** *solubility enhancement (S/S_0) of vanillin in aqueous solutions of ionic hydrotropes (◆) along with the fitted curve (dashed line) obtained using the cooperative hydrotropy model.* ***Right:*** *the linearized form of the cooperative hydrotropy model for each hydrotropic system, where the vertical axis is the left-hand side of Equation S1 and the dashed line is the straight line obtained using the method of least squares. Data measured in this work or taken from the literature.*[4]

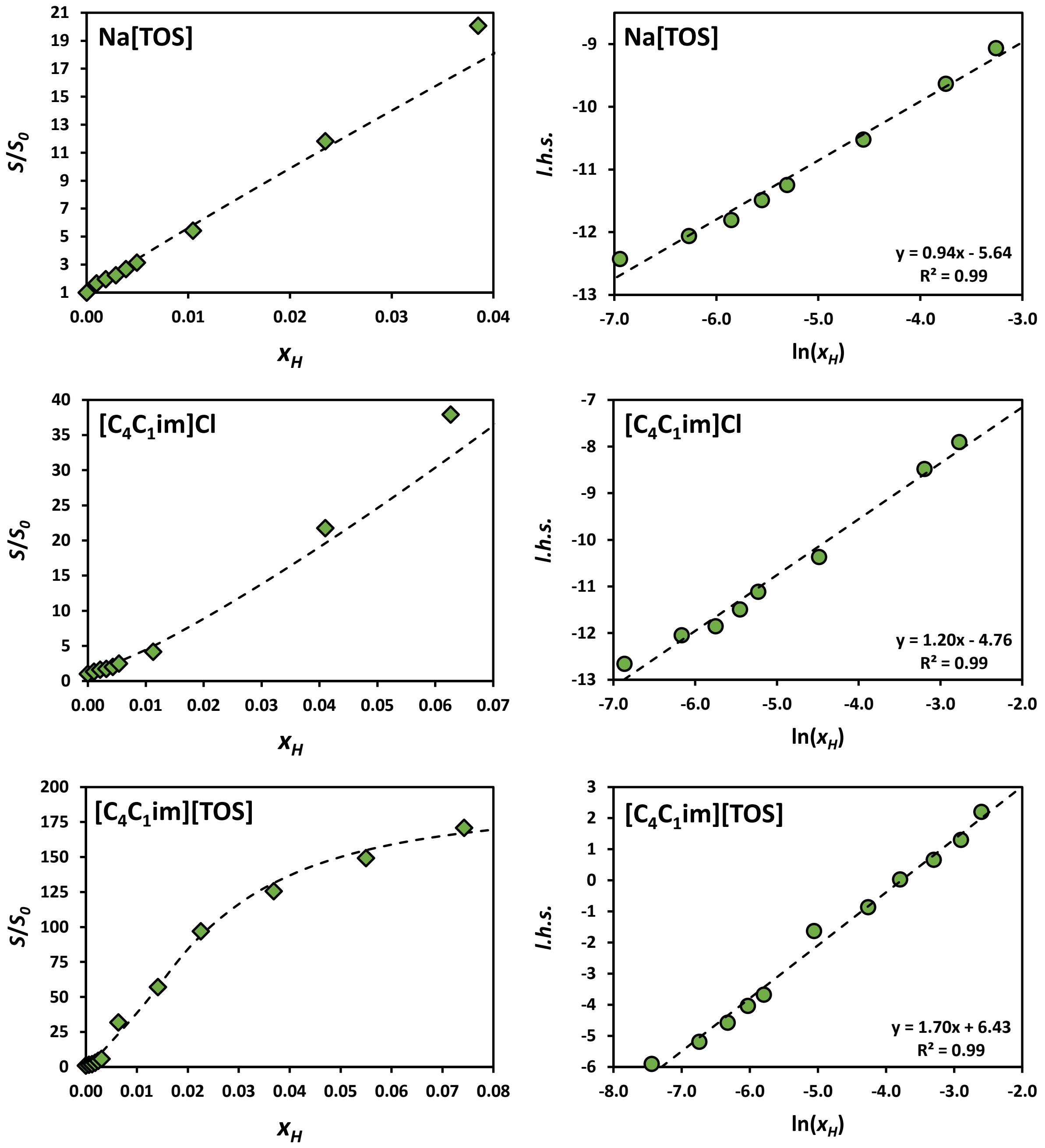

Figure S4. ***Left:*** *solubility enhancement (S/S_0) of syringic acid in aqueous solutions of ionic hydrotropes (◆) along with the fitted curve (dashed line) obtained using the cooperative hydrotropy model.* ***Right:*** *the linearized form of the cooperative hydrotropy model for each hydrotropic system, where the vertical axis is the left-hand side of Equation S1 and the dashed line is the straight line obtained using the method of least squares.*

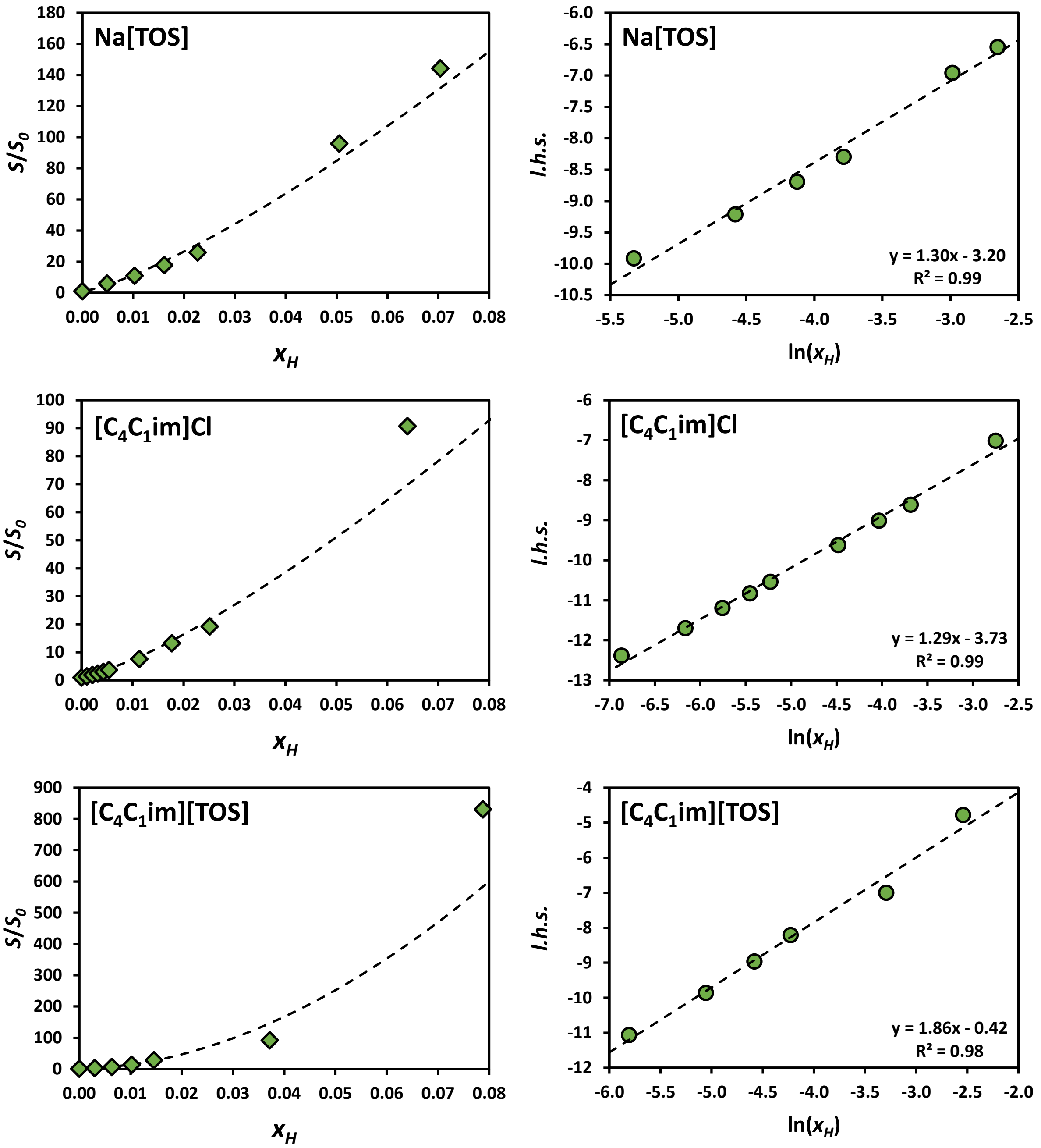

Figure S5. ***Left:*** *solubility enhancement (S/S_0) of naproxen in aqueous solutions of ionic hydrotropes (◆) along with the fitted curve (dashed line) obtained using the cooperative hydrotropy model.* ***Right:*** *the linearized form of the cooperative hydrotropy model for each hydrotropic system, where the vertical axis is the left-hand side of Equation S1 and the dashed line is the straight line obtained using the method of least squares.*

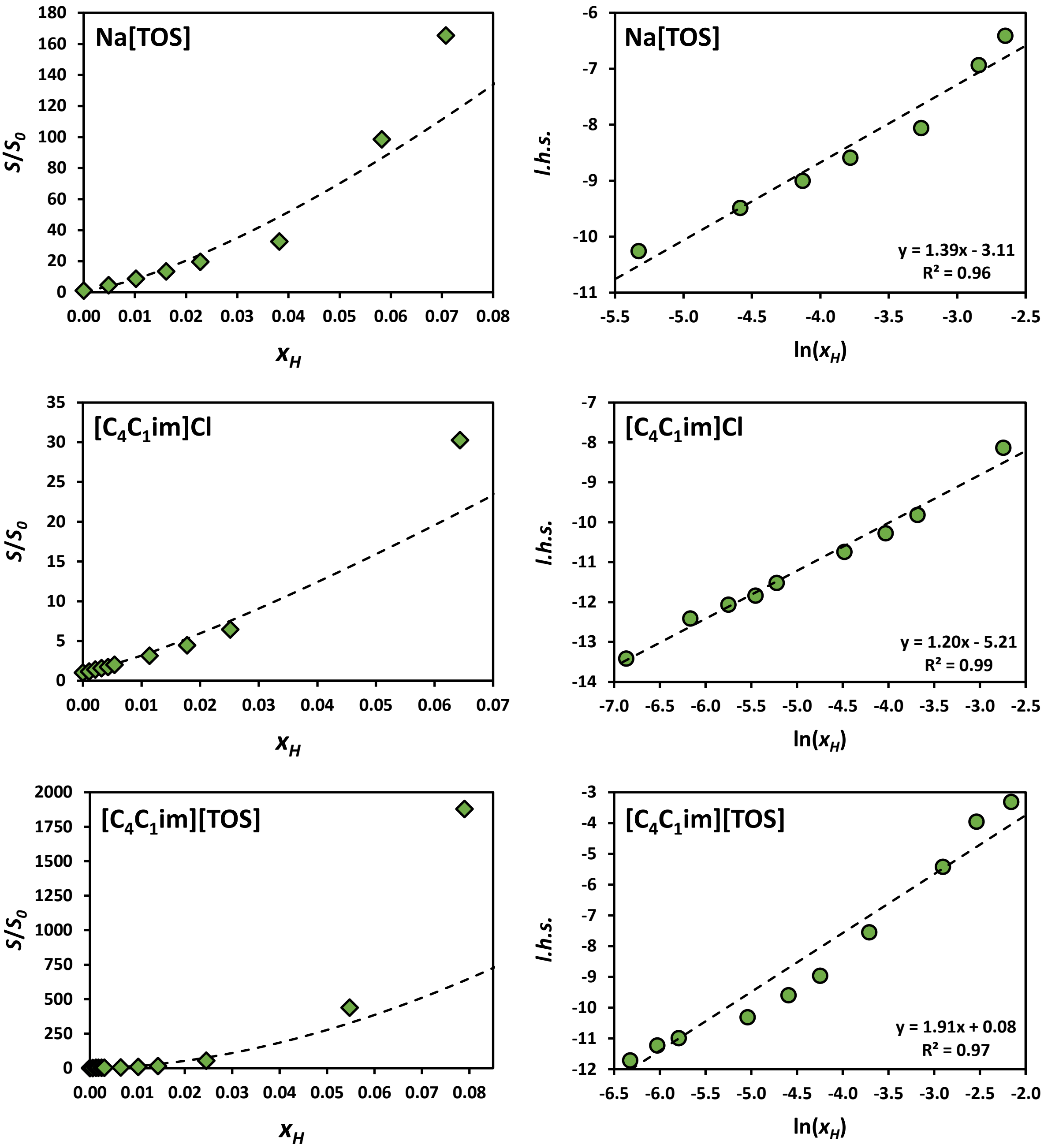

Figure S6. ***Left:*** *solubility enhancement (S/S_0) of ibuprofen in aqueous solutions of ionic hydrotropes (◆) along with the fitted curve (dashed line) obtained using the cooperative hydrotropy model.* ***Right:*** *the linearized form of the cooperative hydrotropy model for each hydrotropic system, where the vertical axis is the left-hand side of Equation S1 and the dashed line is the straight line obtained using the method of least squares. Data measured in this work or taken from the literature.*[5]

Table S11. *Parameters obtained by fitting the cooperative model of hydrotropy to the experimental solubility data analysed in this work.*

	Na[TOS]			$[C_4C_1im]Cl$			$[C_4C_1im][TOS]$		
	m	b	δ_{max}	m	b	δ_{max}	m	b	δ_{max}
Caffeine	0.33	-9.79	**a)**	0.51	-1.57	16	0.82	4.43	3
Gallic Acid	1.60	6.13	4	1.07	2.36	41	1.04	2.93	29
Vanillin	1.41	3.92	32	1.20	-5.16	**a)**	1.09	-4.65	**a)**
Syringic Acid	0.94	-5.64	**a)**	1.20	-4.76	**a)**	1.70	6.43	190
Naproxen	1.30	-3.20	**a)**	1.29	-3.73	**a)**	1.86	-0.42	**a)**
Ibuprofen	1.39	-3.144	**a)**	1.20	-5.21	**a)**	1.83	-0.41	**a)**

a) Unbounded optimization, so the value was set to 100000.

S2.2 Synergistic Effects

To show that the aqueous solubility enhancement by [C_4C_1im][TOS] is not simply the sum of the solubility enhancements due to the presence of Na[TOS] and [C_4C_1im]Cl (S_{sum}), the following relation is defined:

$$S_{sum} - S_0 = \left(S_{Na[TOS]} - S_0\right) + \left(S_{[C_4C_1im]Cl} - S_0\right) \tag{S3}$$

where $S_{Na[TOS]}$ and $S_{[C_4C_1im]Cl}$ are the solubilities of the solute in aqueous Na[TOS] and [C_4C_1im]Cl, respectively. If there were no synergistic effects between the [C_4C_1im] and [TOS] ions, and if the Na and Cl ions did not impact the solubility of the solute, S_{sum} would be equal to the solubility of the solute in aqueous [C_4C_1im][TOS] ($S_{[C_4C_1im][TOS]}$). Note that Equation S3 simplifies to:

$$\left(\frac{S}{S_0}\right)_{sum} = \left(\frac{S}{S_0}\right)_{Na[TOS]} + \left(\frac{S}{S_0}\right)_{[C_4C_1im]Cl} - 1 \tag{S4}$$

where $(S/S_0)_{Na[TOS]}$ and $(S/S_0)_{[C_4C_1im]Cl}$ are the solubility curves of the solute in aqueous solute in aqueous Na[TOS] and [C_4C_1im]Cl, respectively, obtained using the cooperative model of hydrotropy. These fitted curves are depicted in Figure S7.

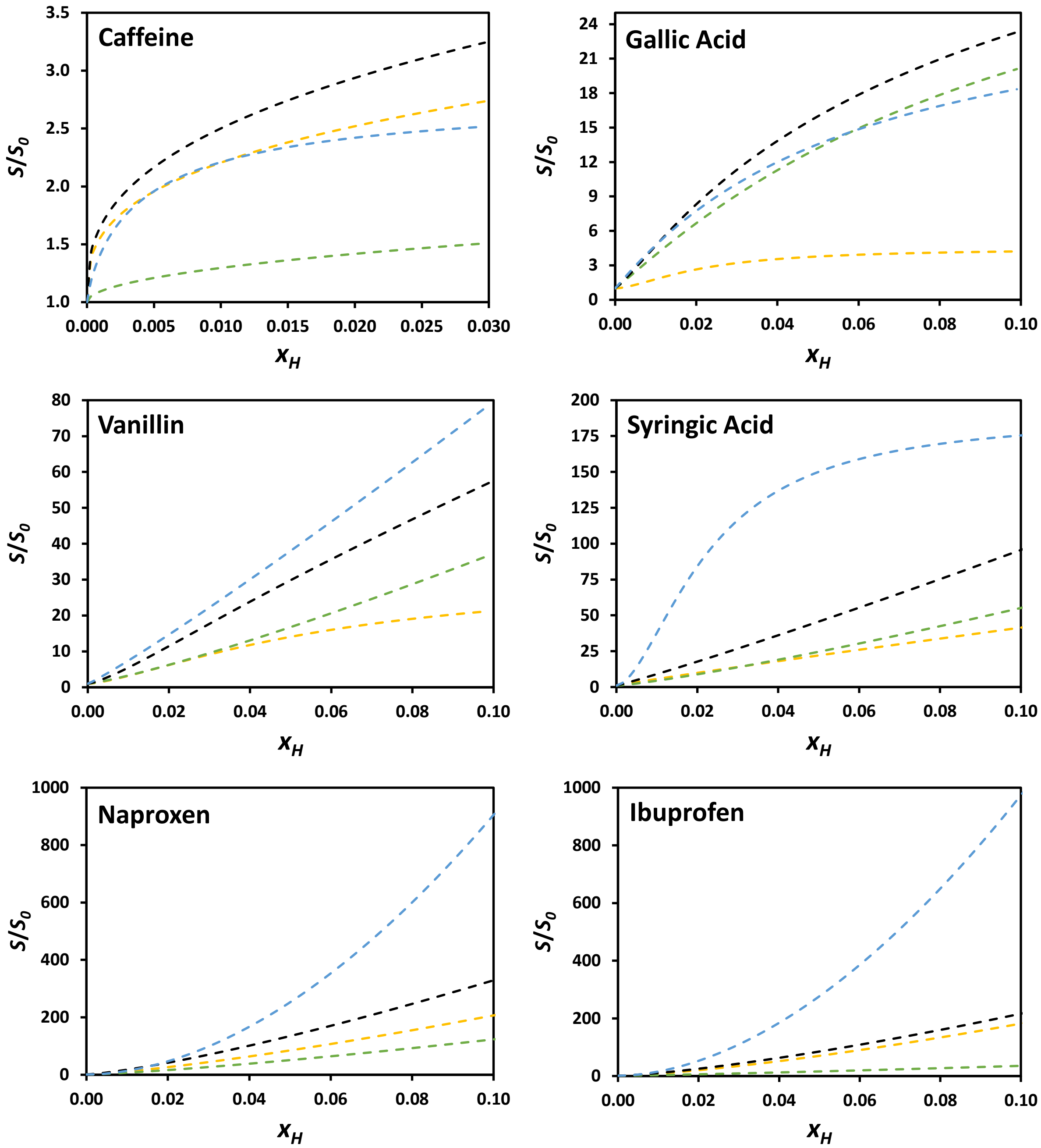

Figure S7. *Solubility curves of the studied solutes in aqueous Na[TOS] (- - -), [C_4C_1im]Cl (- - -), and [C_4C_1im][TOS] (- - -), obtained using the cooperative hydrotropy model, and sum of the solubility curves of the solutes in Na[TOS] and [C_4C_1im]Cl (- - -), obtained using Equation S4.*

S3. Setschenow Constants

The Setschenow constant (K_H) is a parameter used to quantify the ability of an additive to increase the solubility of a solute in a solvent.[6] It can be defined in the following manner:

$$K_H = \frac{d \ln S}{d c_H} \tag{S5}$$

where c_H is the molar concentration of the hydrotrope in the ternary mixture (water/hydrotrope/solute). The Setschenow constant defined as per Equation S5 is linked to the Kirkwood-Buff integrals (KBI) in the following manner:[7]

$$K_H = G_{S,H} - G_{S,W} \tag{S6}$$

where $G_{S,H}$ is the KBI between the solute and the hydrotrope and $G_{S,W}$ is the KBI between the solute and water.

Equation S5 was used to calculate the Setschenow constant of naproxen and ibuprofen in aqueous solutions of [C_4C_1im]Cl, [C_4C_1im][TOS], [C_4C_1im][SCN], and [C_4C_1im][DCA], in the hydrotrope concentration range between 0 and 0.3 M. These results are reported in Table S12 and depicted in Figure S8.

Table S12. *Setschenow constants, defined as per Equation S4, for naproxen and ibuprofen in aqueous solutions of [C_4C_1im]Cl, [C_4C_1im][TOS], [C_4C_1im][SCN], and [C_4C_1im][DCA], taken in the hydrotrope concentration range 0-0.3 M.*

	[C_4C_1im][Cl]	[C_4C_1im][TOS]	[C_4C_1im][SCN]	[C_4C_1im][DCA]
Naproxen	4.75	5.96	9.55	9.66
Ibuprofen	2.46	6.59	9.23	11.48

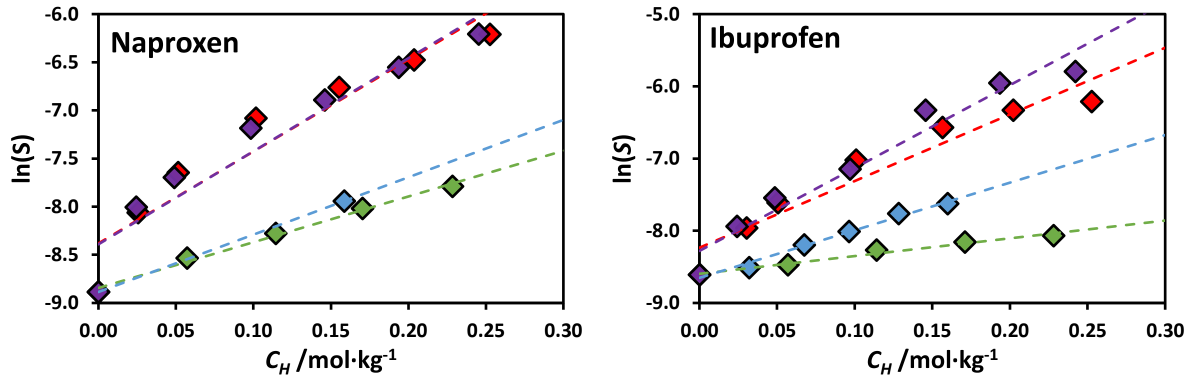

Figure S8. *Aqueous solubility enhancement (S/S0) of naproxen and ibuprofen as a function of the molal concentration (solute-free basis) of [C4C1im]Cl (◆), [C4C1im][TOS] (◆), [C4C1im][SCN] (◆), or [C4C1im][DCA] (◆), at 303.2 K, in the narrow composition range 0-0.3 mol·kg^{-1}. The dashed lines are the straight line obtained using the method of least squares.*

S4. Gibbs Energy of Solvation

To help in rationalizing the impact of the counterion in hydrotropy, the Gibbs solvation energy of the chloride, [TOS], [SCN], and [DCA] anions in water was estimated using the COSMO-RS theory. COSMO-RS is a thermodynamics model that uses a statistical thermodynamics formulation and quantum chemistry descriptions of molecules to calculate the chemical potential of compounds in a liquid mixture. Within the framework of this theory, the Gibbs solvation energy of a compound (ΔG_{solv}) can be estimated using the following expression:

$$\Delta G_{solv} = E_{COSMO} + \mu_{solution}^{\infty} - E_{gas} \tag{S7}$$

where E_{COSMO} and E_{gas} are the quantum chemical total energies of the molecule in the gas phase and the COSMO continuum solvent, respectively, and $\mu_{solution}^{\infty}$ is the chemical potential of the compound in solution at infinite dilution. Note that E_{COSMO} and E_{gas} are obtained from the quantum chemistry descriptions of the compound in the COSMO continuum solvent and in the gas phase, respectively.

The software package COSMOtherm, which implements the COSMO-RS theory, was used in this work with the BP_TZVP_19.ctd parametrization.[8] The geometry, screening charge density and E_{COSMO} of the ions here studied were obtained using the COSMO-BP-TZVP template included in the software package TmoleX (TURBOMOLE).[9] This template optimizes molecules and ions using a def-TZVP basis set for all atoms, a DFT with the B-P86 level of theory, and the COSMO continuum solvation model (infinite permittivity). The gas energy (E_{gas}) was obtained using the GAS-BP-TZVP template of TmoleX, which implements a def-TZVP basis set for all atoms and a DFT with the B-P86 functional.

Equation S7 is equivalent to the difference between the Gibbs energy of the compound in 1 mol of solvent at infinite dilution and the Gibbs energy of the compound in an ideal gas phase at a pressure of 1 bar. To validate this methodology, the Gibbs solvation energy of several common anions in water was calculated and compared against experimental data. Note that numerical equal results between predicted and experimental values are not expected due to the difficulty of computing Gibbs solvation energies for isolated ions.[10] Nevertheless, the values are highly correlated, as Table S13 and Figure S9 show.

Table S13. *Experimental Gibbs energy of solvation (ΔG_{solv})*[11] *and Gibbs energy of solvation ($\Delta G_{COSMO-RS}$) estimated using COSMO-RS for several anions at 298.2 K in water.*

Ion	ΔG_{solv} (kJ·mol^{-1})	$\Delta G_{COSMO-RS}$ (kJ·mol^{-1})	Ion	ΔG_{solv} (kJ·mol^{-1})	$\Delta G_{COSMO-RS}$ (kJ·mol^{-1})
Fluoride (F-)	-439	-442	Azide (N3-)	-296	-314
Chloride (Cl-)	-312	-364	Hydroxide (HO-)	-439	-467
Bromide (Br-)	-287	-339	Peroxide (HO2-)	-407	-431
Iodide (I-)	-251	-307	Formate (HCOO-)	-319	-342
Hypochlorite (ClO-)	-338	-356	Acetate (CH3COO-)	-323	-346
Hypobromide (BrO-)	-318	-345	Benzoate (PhCOO-)	-298	-315
Hypoiodide (IO-)	-299	-337	Mesylate (CH3SO3-)	-300	-320
Cyanide (CN-)	-283	-339	Bisulfide (HS-)	-300	-364

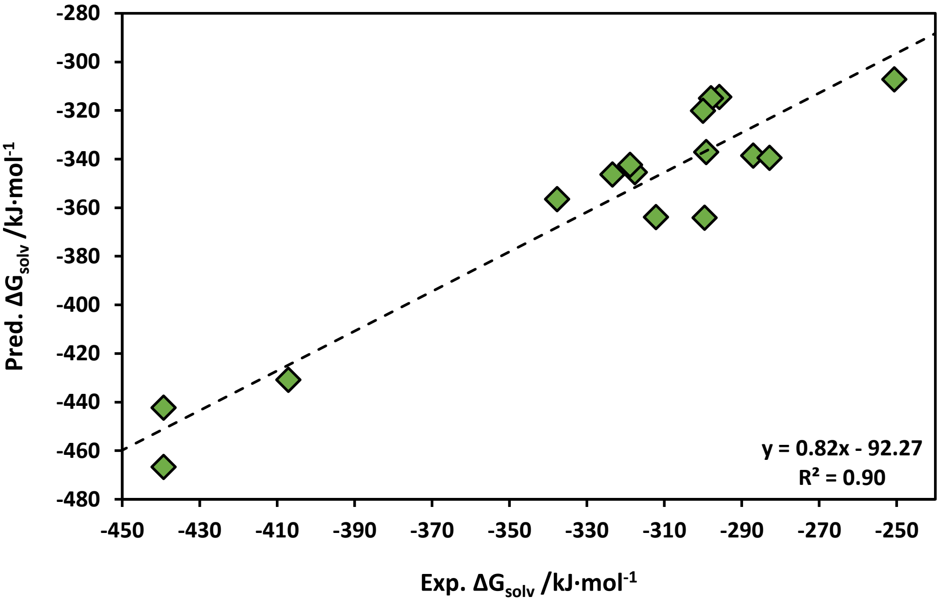

Figure S9. *Correlation between the experimental Gibbs energy of solvation (Exp. ΔG_{solv})*[11] *and the Gibbs energy of solvation (Pred. ΔG_{solv}) estimated using COSMO-RS of several anions at 298.2 K in water.*

The methodology described above was used to estimate the Gibbs hydration energy of the four counterions studied. The values -364 kJ·mol^{-1}, -305 kJ·mol^{-1}, -269 kJ·mol^{-1}, and -255 kJ·mol^{-1} were obtained for chloride, [TOS], [SCN], and [DCA], respectively.

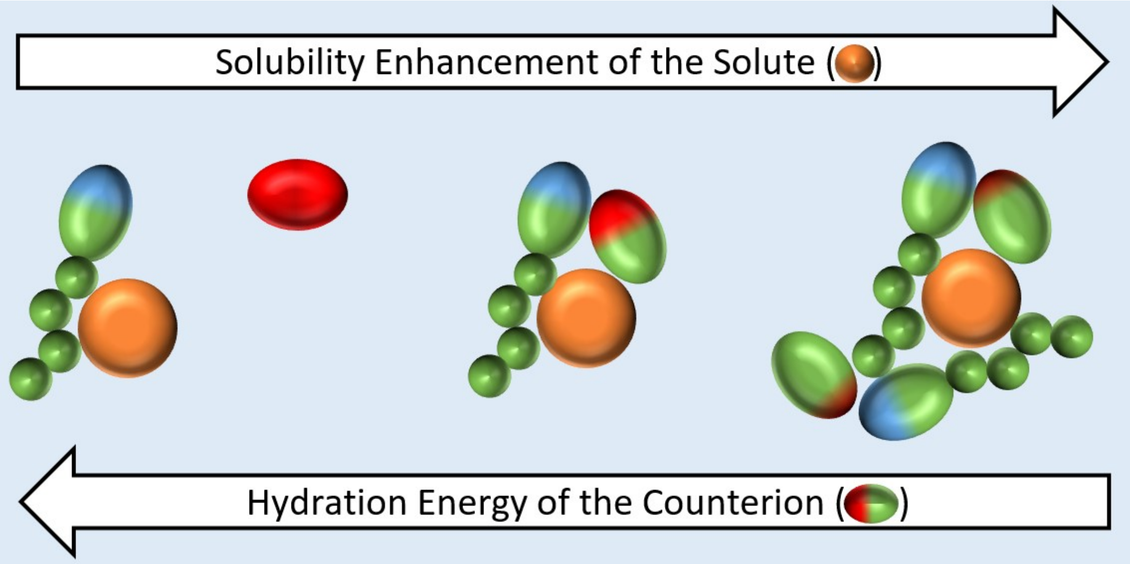

Figure S10. Schematic illustration of the behaviour of the counterion as its Gibbs hydration energy decreases. In the first case the counterion interacts too extensively with water and does not minimize the charge of the hydrotrope-solute cluster, corresponding to the commonly used small, densely charged counterions such as sodium or chloride. In the second and third cases, the counterion is progressively less hydrated and, thus, more available to move into the vicinity of the solute-hydrotrope cluster, minimizing charge repulsion between hydrotrope ions and leading to larger and more stable clusters.

S5. References

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